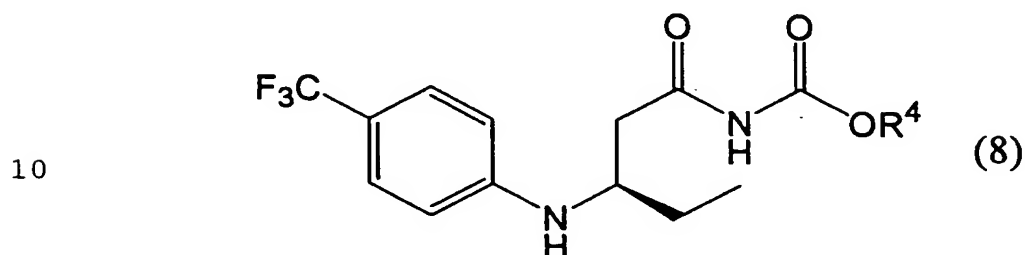


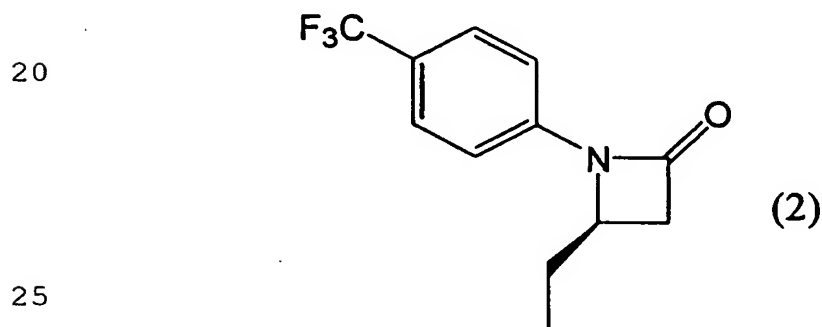
CLAIMS

1. A method for producing an
 (R)-3-[4-(trifluoromethyl)phenylamino]-pentanoic acid amide
 5 derivative defined by the following formula (8):



in the formula, R^4 denotes a C_{1-12} alkyl, a C_{6-12} aryl or a C_{7-12} aralkyl group:

- 15 which comprises reacting
 (R)-4-ethyl-1-[4-(trifluoromethyl)phenyl]-2-azetidinone
 defined by the following formula (2):



with a carbamic acid ester defined by the following formula (9):

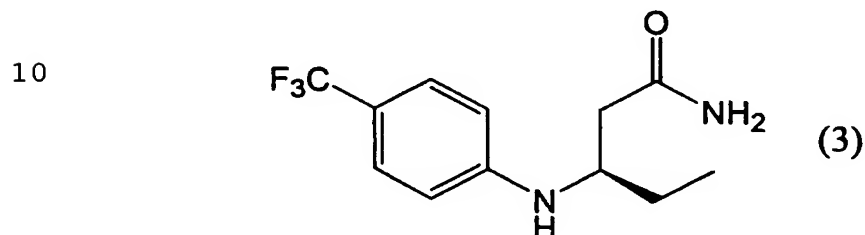


- in the formula, R^4 denotes the same described above:
 30 in the presence of a base.

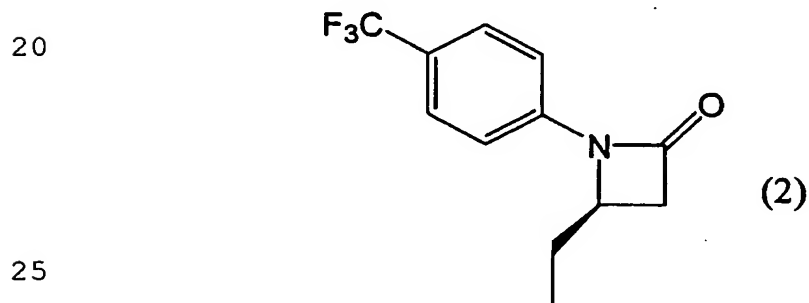
2. The method according to Claim 1,
 wherein R^4 is methyl or benzyl group.
- 35 3. The method according to Claim 1 or 2,

wherein the base is sodium hydride, sodium methoxide, sodium ethoxide, sodium isopropoxide, sodium tert-butoxide, potassium tert-butoxide or lithium tert-butoxide.

- 5 4. A method for producing
(R)-3-[4-(trifluoromethyl)phenylamino]-pentanoic acid amide
defined by the following formula (3):



- 15 which comprises
i) amidation of
(R)-4-ethyl-1-[4-(trifluoromethyl)phenyl]-2-azetidinone
defined by the following formula (2):

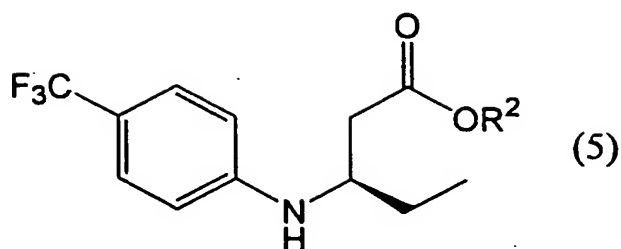


- 25 or
ii) amidation of an
(R)-3-[4-(trifluoromethyl)phenylamino]-pentanoic acid
derivative defined by the following formula (5):

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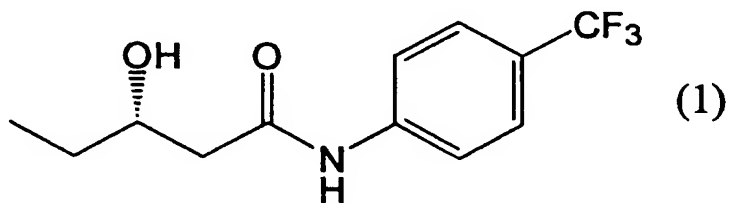


in the formula, R^2 denotes hydrogen atom or a C_{1-5} alkyl group:
 10 obtained by hydrolysis or alcoholysis of the
 (R)-4-ethyl-1-[4-(trifluoromethyl)phenyl]-2-azetidinone
 defined by said formula (2).

15 5. The method according to Claim 4,
 wherein R^2 is hydrogen atom, methyl or ethyl group.

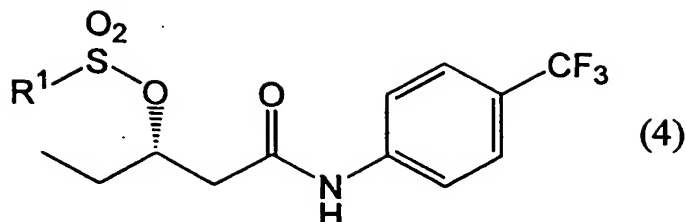
6. The method according to any one of Claims 1 to 5,
 wherein the
 (R)-4-ethyl-1-[4-(trifluoromethyl)phenyl]-2-azetidinone
 20 defined by said formula (2) is produced by
 I) cyclization of
 (S)-N-[4-(trifluoromethyl)phenyl]-3-hydroxypentanoic acid
 amide defined by the following formula (1):

25



30 with a dehydration condensing agent, or
 II) a production of an
 (S)-N-[4-(trifluoromethyl)phenyl]-3-sulfonyloxypentanoic
 acid amide derivative defined by the following formula (4):

35



in the formula, R^1 denotes a C_{1-12} alkyl group optionally having a substituent or a C_{6-12} aryl group optionally having a substituent:

by sulfonylation of the
(S)-N-[4-(trifluoromethyl)phenyl]-3-hydroxypentanoic acid
amide defined by said formula (1), and successive treatment with
a base.

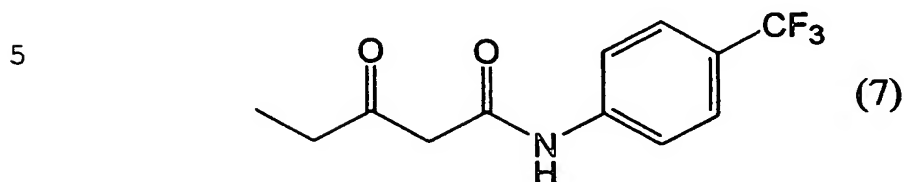
7. The method according to Claim 6,
wherein the dehydration condensing agent is a combination
of at least one azo compound selected from dimethyl
azodicarboxylate, diethyl azodicarboxylate and diisopropyl
azodicarboxylate, and at least one phosphine compound selected
from tri-n-butylphosphine, tricyclohexylphosphine and
triphenylphosphine.

8. The method according to Claim 6,
wherein R^1 is methyl or 4-methylphenyl group.

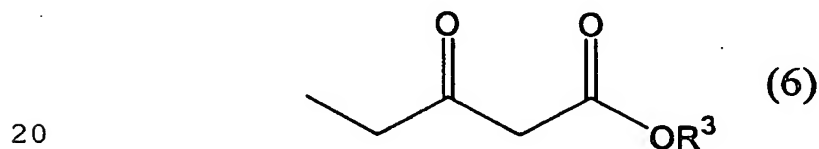
9. The method according to Claim 6 or 8,
wherein the base is sodium hydride, sodium methoxide,
sodium ethoxide, sodium isopropoxide, sodium tert-butoxide,
potassium tert-butoxide, lithium tert-butoxide, sodium
hydroxide or potassium hydroxide.

10. The method according to any one of Claims 6 to 9,
wherein the
(S)-N-[4-(trifluoromethyl)phenyl]-3-hydroxypentanoic acid
amide defined by said formula (1) is produced by asymmetric

reduction of N-[4-(trifluoromethyl)phenyl]-3-oxopentanoic acid amide defined by the following formula (7):



10 11. The method according to Claim 10,
 wherein the
N-[4-(trifluoromethyl)phenyl]-3-oxopentanoic acid amide
defined by said formula (7) is produced by a reaction of a
3-oxopentanoic acid ester derivative defined by the following
15 formula (6):



in the formula, R^3 denotes a C_{1-5} alkyl group:
and 4-(trifluoromethyl)aniline.

25 12. The method according to Claim 11,
 wherein R^3 is methyl or ethyl group.

 13. The method according to any one of Claims 10 to 12,
 wherein the asymmetric reduction of the
30 N-[4-(trifluoromethyl)phenyl]-3-oxopentanoic acid amide
defined by said formula (7) is carried out in the presence of
an asymmetric transition metal catalyst.

 14. The method according to Claim 13,
35 wherein the asymmetric transition metal catalyst is

((S)-BINAP)RuBr₂, ((S)-BINAP)RuCl₂ or [((S)-BINAP)RuCl₂]₂NEt₃, wherein BINAP is 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl).

5 15. The method according to any one of Claims 10 to 12, wherein the asymmetric reduction of the N-[4-(trifluoromethyl)phenyl]-3-oxopentanoic acid amide defined by said formula (7) is carried out by using an enzyme source having activity of stereoselectively reducing the
10 N-[4-(trifluoromethyl)phenyl]-3-oxopentanoic acid amide.

 16. The method according to Claim 15, wherein the enzyme source is an enzyme obtainable from a cultured product of a microorganism selected from the group
15 consisting of Arthrobacter, Bacillus, Brevibacterium, Clostridium, Corynebacterium, Flavobacterium, Luteococcus, Microbacterium, Pseudomonas, Paenibacillus, Serratia, Nocardia, Rathayibacter, Rhodococcus, Candida and Cryptococcus, and/or from the microorganism.

20 17. The method according to Claim 16, wherein the enzyme source is an enzyme obtainable from a cultured product of a microorganism selected from the group consisting of Arthrobacter paraffineus, Bacillus cereus,
25 Bacillus subtilis, Bacillus amyloliquefaciens, Bacillus licheniformis, Brevibacterium iodinum, Clostridium cylindrosporum, Corynebacterium flavesceus, Corynebacterium xerosis, Flavobacterium flavesceus, Luteococcus japonicus, Microbacterium lacticum, Pseudomonas stutzeri, Pseudomonas
30 fluoresceus, Paenibacillus amylolyticus, Paenibacillus polymyxa, Paenibacillus alvei, Serratia marcescens, Nocardia globerula, Rathayibacter rathayi, Rhodococcus erythropolis, Candida guilliermondii, Candida intermedia, Candida molischiana and Cryptococcus albidus, and/or from the
35 microorganism.

18. A method for producing an
(R)-3-[4-(trifluoromethyl)phenylamino]-pentanoic acid amide
derivative defined by said formula (8)

5 which comprises reacting the
(R)-3-[4-(trifluoromethyl)phenylamino]-pentanoic acid amide
defined by said formula (3) produced by the method according
to any one of Claims 4 to 17 with a chlorocarbonic acid ester
defined by the following formula (10):

10 ClCOOR^4 (10)

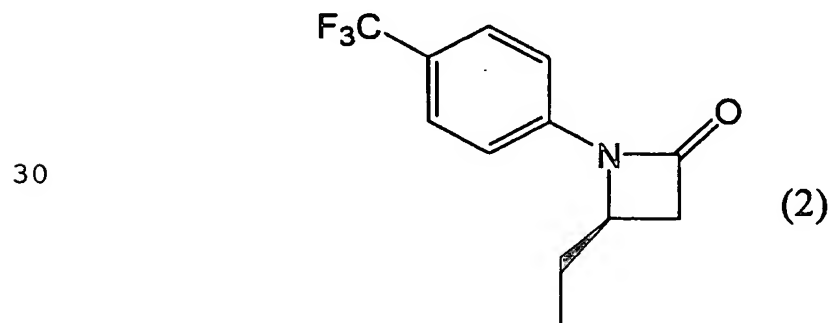
in the formula, R^4 denotes a C_{1-12} alkyl, a C_{6-12} aryl or a C_{7-12}
aralkyl group:

in the presence of a base.

15 19. The method according to Claim 18,
wherein R^4 is methyl or benzyl group.

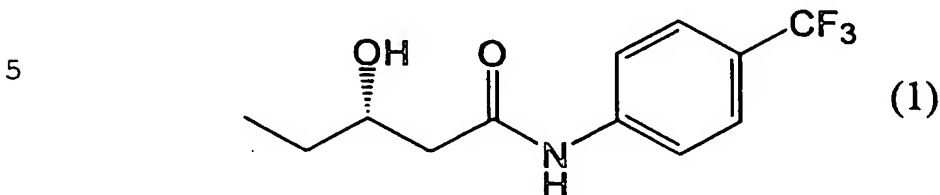
20. The method according to Claim 18 or 19,
wherein the base is sodium hydride, sodium methoxide,
20 sodium ethoxide, sodium isopropoxide, sodium tert-butoxide,
potassium tert-butoxide or lithium tert-butoxide.

21. A method for producing
(R)-4-ethyl-1-[4-(trifluoromethyl)phenyl]-2-azetidinone
25 defined by the following formula (2):



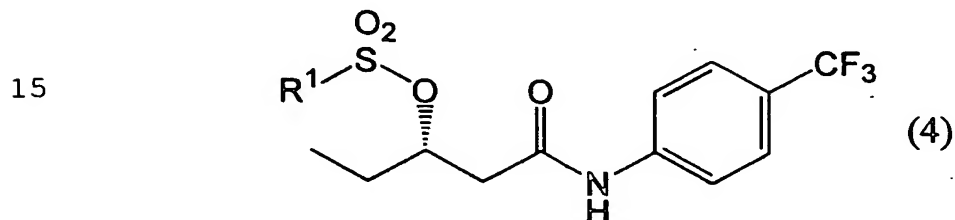
35 which comprises
I) cyclization of

(S)-N-[4-(trifluoromethyl)phenyl]-3-hydroxypentanoic acid amide defined by the following formula (1):



with a dehydration condensing agent, or

10 II) a production of an
(S)-N-[4-(trifluoromethyl)phenyl]-3-sulfonyloxypentanoic acid amide derivative defined by the following formula (4):



20 in the formula, R¹ denotes a C₁₋₁₂ alkyl group optionally having a substituent or a C₆₋₁₂ aryl group optionally having a substituent:

by sulfonylation of the
(S)-N-[4-(trifluoromethyl)phenyl]-3-hydroxypentanoic acid amide defined by said formula (1), and successive treatment with
25 a base.

22. The method according to Claim 21,
wherein the dehydration condensing agent is a combination
of at least one azo compound selected from dimethyl
30 azodicarboxylate, diethyl azodicarboxylate and diisopropyl azodicarboxylate, and at least one phosphine compound selected from tri-n-butylphosphine, tricyclohexylphosphine and triphenylphosphine.

35 23. The method according to Claim 21,

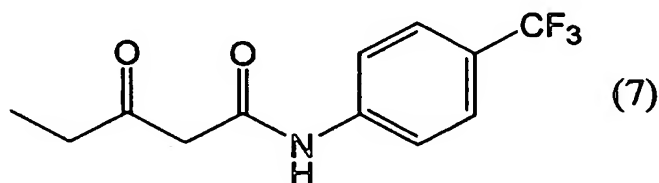
wherein R^1 is methyl or 4-methylphenyl group.

24. The method according to Claim 21 or 23,

wherein the base is sodium hydride, sodium methoxide,
5 sodium ethoxide, sodium isopropoxide, sodium tert-butoxide,
potassium tert-butoxide, lithium tert-butoxide, sodium
hydroxide or potassium hydroxide.

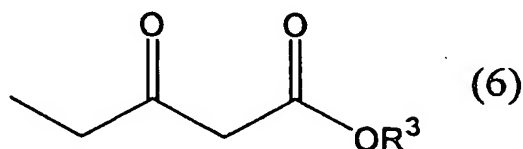
25. The method according to any one of Claims 21 to 24,
10 wherein the

(S)-N-[4-(trifluoromethyl)phenyl]-3-hydroxypentanoic acid
amide defined by said formula (1) is produced by asymmetric
reduction of N-[4-(trifluoromethyl)phenyl]-3-oxopentanoic
acid amide defined by the following formula (7):



26. The method according to Claim 25,
wherein the

N-[4-(trifluoromethyl)phenyl]-3-oxopentanoic acid amide
25 defined by said formula (7) is produced by a reaction of a
3-oxopentanoic acid ester derivative defined by the following
formula (6):



in the formula, R^3 denotes a C_{1-5} alkyl group:
35 and 4-(trifluoromethyl)aniline.

27. The method according to Claim 26,
wherein R³ is methyl or ethyl group.

5 28. The method according to any one of Claims 25 to 27,
 wherein the asymmetric reduction of the
N-[4-(trifluoromethyl)phenyl]-3-oxopentanoic acid amide
defined by said formula (7) is carried out in the presence of
an asymmetric transition metal catalyst.

10 29. The method according to Claim 28,
 wherein the asymmetric transition metal catalyst is
((S)-BINAP)RuBr₂, ((S)-BINAP)RuCl₂ or [((S)-BINAP)RuCl₂]₂NEt₃,
wherein BINAP is
15 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl).

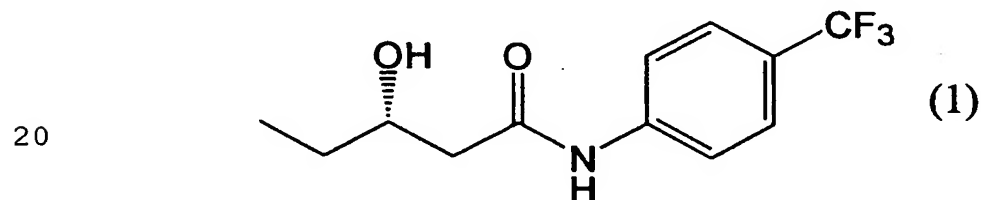
 30. The method according to any one of Claims 25 to 27,
 wherein the asymmetric reduction of the
N-[4-(trifluoromethyl)phenyl]-3-oxopentanoic acid amide
20 defined by said formula (7) is carried out by using an enzyme
source having activity of stereoselectively reducing the
N-[4-(trifluoromethyl)phenyl]-3-oxopentanoic acid amide.

 31. The method according to Claim 30,
25 wherein the enzyme source is an enzyme obtainable from
a cultured product of a microorganism selected from the group
consisting of Arthrobacter, Bacillus, Brevibacterium,
Clostridium, Corynebacterium, Flavobacterium, Luteococcus,
Microbacterium, Pseudomonas, Paenibacillus, Serratia,
30 Nocardia, Rathayibacter, Rhodococcus, Candida and
Cryptococcus, and/or from the microorganism.

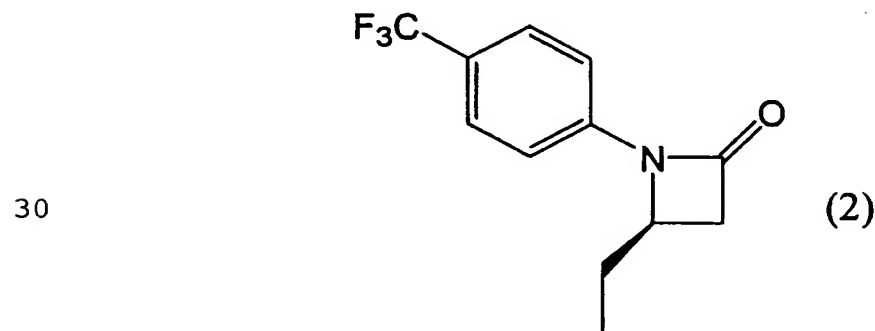
 32. The method according to Claim 31,
 wherein the enzyme source is an enzyme obtainable from
35 a cultured product of a microorganism selected from the group

consisting of *Arthrobacter paraffineus*, *Bacillus cereus*,
Bacillus subtilis, *Bacillus amyloliquefaciens*, *Bacillus*
licheniformis, *Brevibacterium iodinum*, *Clostridium*
cylindrosporum, *Corynebacterium flavescens*, *Corynebacterium*
 5 *xerosis*, *Flavobacterium flavescens*, *Luteococcus japonicus*,
Microbacterium lacticum, *Pseudomonas stutzeri*, *Pseudomonas*
fluorescens, *Paenibacillus amylolyticus*, *Paenibacillus*
polymyxa, *Paenibacillus alvei*, *Serratia marcescens*, *Nocardia*
globerula, *Rathayibacter rathayi*, *Rhodococcus erythropolis*,
 10 *Candida guilliermondii*, *Candida intermedia*, *Candida*
molischiana and *Cryptococcus albidus*, and/or from the
 microorganism.

33. (S)-N-[4-(trifluoromethyl)phenyl]-3-
 15 hydroxypentanoic acid amide defined by the following formula
 (1):

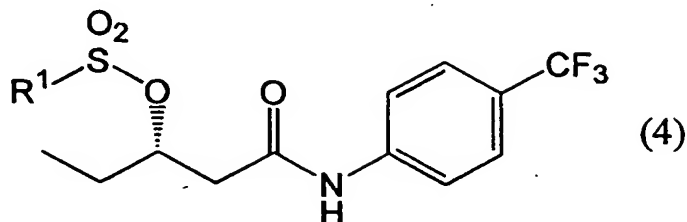


34. (R)-4-ethyl-1-[4-(trifluoromethyl)phenyl]-2-
 25 azetidinone defined by the following formula (2):



35 An (S)-N-[4-(trifluoromethyl)phenyl]-3-

sulfonyloxypentanoic acid amide derivative defined by the following formula (4):

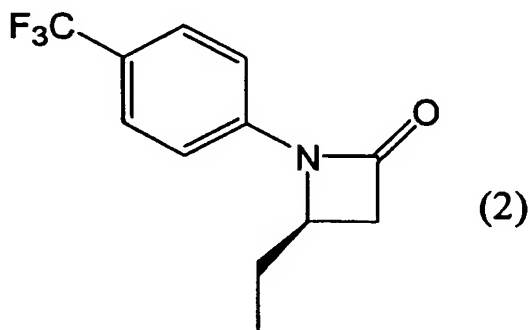


10 in the formula, R^1 denotes a C_{1-12} alkyl group optionally having a substituent or a C_{6-12} aryl group optionally having a substituent.

15 36. The (S)-N-[4-(trifluoromethyl)phenyl]-3-sulfonyloxypentanoic acid amide derivative according to Claim 35,

wherein R^1 is methyl or 4-methylphenyl group.

20 37. A method for isolating and purifying (R)-4-ethyl-1-[4-(trifluoromethyl)phenyl]-2-azetidinone defined by the following formula (2):



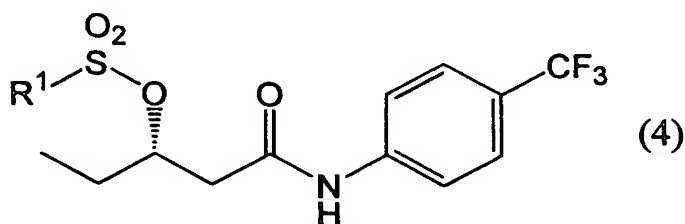
30 which comprises removing a contaminating (S)-4-ethyl-1-[4-(trifluoromethyl)phenyl]-2-azetidinone by crystallization from a hydrocarbon solvent to obtain the (R)-4-ethyl-1-[4-(trifluoromethyl)phenyl]-2-azetidinone as a crystal with improved optical purity.

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38. The method according to Claim 37,
wherein the hydrocarbon solvent is hexane, heptane or
methylcyclohexane.

39. The method according to Claim 37 or 38,
wherein the
(R)-4-ethyl-1-[4-(trifluoromethyl)phenyl]-2-azetidinone
defined by said formula (2) produced by the method according
to any one of Claims 21 to 32 is used.

40. A method for isolating and purifying an
(S)-N-[4-(trifluoromethyl)phenyl]-3-sulfonyloxypentanoic
acid amide derivative defined by the following formula (4):



in the formula, R^1 denotes a C_{1-12} alkyl group optionally having
a substituent or a C_{6-12} aryl group optionally having a
substituent:

which comprises removing a contaminating
(R)-N-[4-(trifluoromethyl)phenyl]-3-sulfonyloxypentanoic
acid amide derivative by crystallization from an aromatic
hydrocarbon solvent to obtain an
(S)-N-[4-(trifluoromethyl)phenyl]-3-sulfonyloxypentanoic
acid amide derivative as a crystal with improved optical purity.

41. The method according to Claim 40,
wherein R^1 is methyl group.

42. The method according to Claim 40 or 41,
wherein the aromatic hydrocarbon solvent is at least one
species selected among benzene, toluene, o-xylene, m-xylene,

p-xylene, 1,3,5-mesitylene and cumene.

43. The method according to any one of Claims 40 to 42,
wherein the (S)-N-[4-(trifluoromethyl)phenyl]-3-
5 sulfonyloxypentanoic acid amide derivative defined by said
formula (4) is crystallized by further using an auxiliary
solvent in order to improve at least one among the yield of the
compound (4), the treatment concentration of the compound (4),
the liquid property of the compound (4) and the physical
10 property of the crystal to be obtained.

44. The method according to any one of Claims 40 to 43,
wherein the auxiliary solvent is at least one species
selected among pentane, hexane, heptane, cyclohexane,
15 methylcyclohexane, octane and isooctane.

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